EWS-FLI1 causes neuroepithelial defects and abrogates emigration of neural crest stem cells.

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Authors: Edward G Coles, Elizabeth R Lawlor, Marianne Bronner-Fraser

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Public Summary:

Scientific Abstract:
The most frequently occurring chromosomal translocation that gives rise to the Ewing's sarcoma family of tumors (ESFT) is the chimeric fusion gene EWS-FLI1 that encodes an oncogenic protein composed of the N terminus of EWS and the C terminus of FLI1. Although the genetic basis of ESFT is fairly well understood, its putative cellular origin remains to be determined. Previous work has proposed that neural crest progenitor cells may be the causative cell type responsible for ESFT. However, surprisingly little is known about the expression pattern or role of either wild-type EWS or wild-type FLI1 in this cell population during early embryonic development. Using the developing chick embryo as a model system, we identified EWS expression in emigrating and migratory neural crest stem cells, whereas FLI1 transcripts were found to be absent in these populations and were restricted to developing endothelial cells. By ectopically expressing EWS-FLI1 or wild-type FLI1 in the developing embryo, we have been able to study the cellular transformations that ensue in the context of an in vivo model system. Our results reveal that misexpression of the chimeric EWS-FLI1 fusion gene, or wild-type FLI1, in the developing neural crest stem cell population leads to significant aberrations in neural crest development. An intriguing possibility is that misexpression of the EWS-FLI1 oncogene in neural crest-derived stem cells may be an initiating event in ESFT genesis.